# STIC Search Report
## Biotech-Chem Library

STIC Database Tracking Number: 146255

| | |
|---|---|
| **TO: Kahsay Habte**<br>**Location: 5c15/c18**<br>**Art Unit: 1624**<br>**Wednesday, March 02, 2005**<br><br>**Case Serial Number: 10/716027** | **From: Noble Jarrell**<br>**Location: Biotech-Chem Library**<br>**Rem 1B71**<br>**Phone: 272-2556**<br><br>**Noble.jarrell@uspto.gov** |

## Search Notes

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=> d his

     (FILE 'HOME' ENTERED AT 10:06:58 ON 02 MAR 2005)

     FILE 'HCAPLUS' ENTERED AT 10:07:07 ON 02 MAR 2005
L1            1 US20040152701/PN
               E IN2002-MAS898/AP,PRN

     FILE 'REGISTRY' ENTERED AT 10:07:59 ON 02 MAR 2005

     FILE 'HCAPLUS' ENTERED AT 10:08:01 ON 02 MAR 2005
L2              TRA L1 1- RN :        3 TERMS

     FILE 'REGISTRY' ENTERED AT 10:08:01 ON 02 MAR 2005
L3            3 SEA L2

     FILE 'WPIX' ENTERED AT 10:08:06 ON 02 MAR 2005
L4            1 US20040152701/PN
              E IN2002-MAS898/AP,PRN

=> b hcap
FILE 'HCAPLUS' ENTERED AT 10:08:42 ON 02 MAR 2005
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FILE COVERS 1907 - 2 Mar 2005  VOL 142 ISS 10
FILE LAST UPDATED: 1 Mar 2005  (20050301/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d all l1

L1   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:633285  HCAPLUS
DN   141:162476
ED   Entered STN:  06 Aug 2004
TI   Novel anhydrous crystalline form of Levofloxacin and process for its
     preparation
IN   Reddy, Manne Satyanarayana; Eswaraiah, Sajja; Reddy, Koppera Ravinder;
     Reddy, Maram Reddy Sahadeva; Prakash, Pitta Jaya
PA   Reddy's Laboratories Limited, India; Reddy's Laboratories, Inc.
SO   U.S. Pat. Appl. Publ., 6 pp.
     CODEN: USXXCO
DT   Patent
LA   English
IC   ICM  A61K031-58
     ICS  C07D491-02
NCL  514230500: 544105000
CC   63-8 (Pharmaceuticals)
     Section cross-reference(s): 28
```

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004152701 | A1 | 20040805 | US 2003-716207 | 20031118 <-- |
| PRAI | IN 2002-MA898 | A | 20021202 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| US 2004152701 | ICM | A61K031-58 |
| | ICS | C07D491-02 |
| | NCL | 514230500; 544105000 |
| US 2004152701 | ECLA | C07D498/04+265C+221C <-- |

AB A process for the preparation of an anhydrous crystalline form of an antimicrobial agent Levofloxacin comprises the condensation of N-methyl-piperazine with S(-)-9,10-difluoro-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de]-[1,4]-benzoxazine-6-carboxylic acid in acetonitrile followed by distillation of solvent to afford the residue, the resultant residue is refluxed with toluene and the solid is filtered at room temperature to afford the Levofloxacin. Levofloxacin was further refluxed in acetonitrile, filtered and dried to constant weight to give the anhydrous crystalline form of Levofloxacin. The anhydrous crystalline form of Levofloxacin is characterized by X-ray diffractogram, Differential Scanning Calorimetry thermogram and IR Spectra. 1.

ST levofloxacin anhyd cryst form prepn

IT 100986-85-4P, Levofloxacin
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of anhydrous crystalline form of levofloxacin)

IT 109-01-3, N-Methylpiperazine 100986-89-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of anhydrous crystalline form of levofloxacin)

=> b reg
FILE 'REGISTRY' ENTERED AT 10:08:47 ON 02 MAR 2005
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 FEB 2005 HIGHEST RN 839671-97-5
DICTIONARY FILE UPDATES: 28 FEB 2005 HIGHEST RN 839671-97-5

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

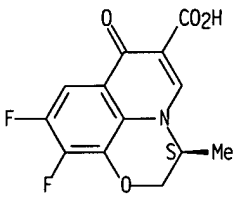
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide l3 tot

L3 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
RN **100986-89-8** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9,10-difluoro-2,3-dihydro-3-methyl-7-oxo-, (3S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,

9,10-difluoro-2,3-dihydro-3-methyl-7-oxo-, (S)-
OTHER NAMES:
CN 9,10-Difluoro-3-(S)-methyl-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid
FS STEREOSEARCH
MF C13 H9 F2 N O4
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMCATS, PS, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry. Rotation (-).



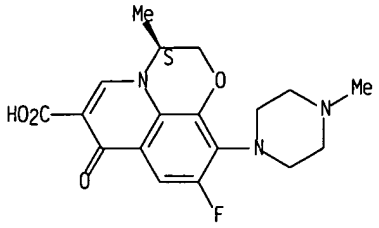

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

53 REFERENCES IN FILE CA (1907 TO DATE)
53 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
RN **100986-85-4** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (S)-
OTHER NAMES:
CN (-)-Ofloxacin
CN (S)-(-)-Ofloxacin
CN (S)-Ofloxacin
CN Cravit
CN DR 3355
CN HR 355
CN Levaquin
CN Levofloxacin
CN Quixin
CN RWJ 25213-097
CN Tavanic
FS STEREOSEARCH
MF C18 H20 F N3 O4
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL

(*File contains numerically searchable property data)
DT.CA CAplus document type: Book; Conference; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry. Rotation (-).

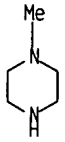



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2186 REFERENCES IN FILE CA (1907 TO DATE)
18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2200 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L3 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2005 ACS on STN
RN **109-01-3** REGISTRY
CN Piperazine, 1-methyl- (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-Methylpiperazine
CN N-Methylpiperazine
CN NSC 30195
CN NSC 30675
FS 3D CONCORD
MF C5 H12 N2
CI COM
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CSCHEM, DETHERM*, EMBASE, GMELIN*, HODOC*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MSDS-OHS, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Journal; Patent; Preprint; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); CMBI (Combinatorial study); FORM (Formation, nonpreparative);

OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

5777 REFERENCES IN FILE CA (1907 TO DATE)
90 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5805 REFERENCES IN FILE CAPLUS (1907 TO DATE)
15 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> b wpix
FILE 'WPIX' ENTERED AT 10:08:51 ON 02 MAR 2005
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FILE LAST UPDATED: 28 FEB 2005 <20050228/UP>
MOST RECENT DERWENT UPDATE: 200514 <200514/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
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>>> SMILES and ISOSMILES strings are no longer available as Derwent Chemistry Resource display fields <<<

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=> d all l4

L4 ANSWER 1 OF 1 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2004-570747 [55] WPIX
DNC C2004-208424

TI New anhydrous crystalline form of S (-)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido(1,2,3-de)-1,4-benzoxazine-6-carboxylic acid, used for treating infections caused by bacteria.
DC B02
IN ESWARAIAH, S; PRAKASH, P J; REDDY, K R; REDDY, M R S; REDDY, M S
PA (REDD-N) REDDY'S LAB LTD
CYC 1
PI US 2004152701 A1 20040805 (200455)* 6 A61K031-58 <--
ADT US 2004152701 A1 US 2003-716207 20031118
PRAI IN 2002-CH898 20021202
IC ICM A61K031-58
ICS C07D491-02
AB US2004152701 A UPAB: 20040826
NOVELTY - Anhydrous crystalline form of S (-)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido(1,2,3-de)-1,4-benzoxazine-6-carboxylic acid (levofloxacin) (I), is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the preparation of (I)

ACTIVITY - Antimicrobial; Antibacterial.

No biological data is given.

MECHANISM OF ACTION - None given.

USE - (I) is a quinolone antibiotic used for treating treat lung, skin and urinary tract infections caused by bacteria.

ADVANTAGE - (I) Is a free flowing and non-solvated crystalline solid, so that it is suitable for pharmaceutical formulations. (I) is characterized by a X-ray diffractogram and the pattern is different from any of the other hydrate forms of levofloxacin. Preparation of (I) is a simple, environmentally friendly and commercially viable process.

Dwg.0/2
FS CPI
FA AB; DCN
MC CPI: B02-L; B06-E05; B12-M11H; B14-A01; B14-K01; B14-N07; B14-N17

=> b home
FILE 'HOME' ENTERED AT 10:08:55 ON 02 MAR 2005

=>

=> b reg
FILE 'REGISTRY' ENTERED AT 10:23:32 ON 02 MAR 2005


Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES: 1 MAR 2005 HIGHEST RN 840454-17-3
DICTIONARY FILE UPDATES: 1 MAR 2005 HIGHEST RN 840454-17-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

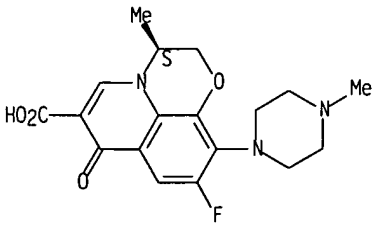
=> d ide l13 tot

L13 ANSWER 1 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **836608-80-1** REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF **C18 H20 F N3 O4 . C3 H6 O3 . 1/2 H2 O**
SR CA
LC STN Files: CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: BIOL (Biological study); USES (Uses)

CM 1

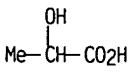
CRN 100986-85-4
CMF C18 H20 F N3 O4

Absolute stereochemistry. Rotation (-).




CM 2

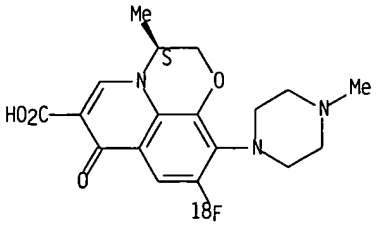
CRN 50-21-5
CMF C3 H6 O3



1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 2 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **637328-10-0** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,
9-(fluoro-18F)-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-,
(3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H20 F N3 O4**
SR CA
LC STN Files: CA, CAPLUS, CASREACT
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation)

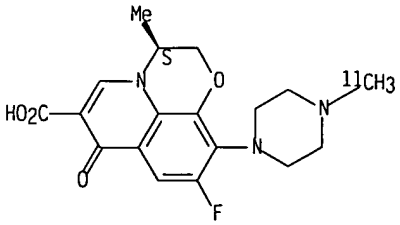
Absolute stereochemistry.




1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 3 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **403655-77-6** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,
9-fluoro-2,3-dihydro-3-methyl-10-[4-(methyl-11C)-1-piperazinyl]-7-oxo-,
(3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H20 F N3 O4**
SR CA
LC STN Files: CA, CAPLUS, CASREACT
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation)

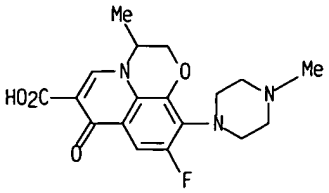
Absolute stereochemistry.




1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 4 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **362677-88-1** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,
9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-,
conjugate monoacid (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Ofloxacin, monoprotonated
MF **C18 H20 F N3 O4 . H**

SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PROC (Process); PRP (Properties)
CRN (82419-36-1)



2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 5 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **352465-40-8** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, nitrate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Ofloxacin nitrate
MF **C18 H20 F N3 O4 . x H N O3**
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

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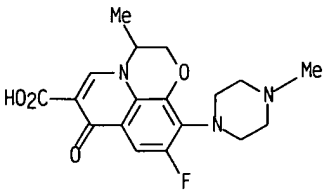
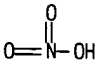
CRN 82419-36-1
CMF C18 H20 F N3 O4



CM 2

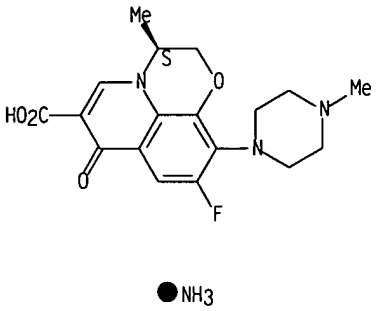
CRN 7697-37-2
CMF H N O3



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 6 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **346607-44-1** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, ammonium salt, (3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H20 F N3 O4 . H3 N**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
CRN (100986-85-4)

Absolute stereochemistry. Rotation (-).

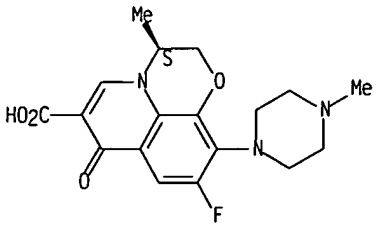



● $NH_3$

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 7 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **346607-39-4** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, hydrobromide, (3S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H20 F N3 O4 . x Br H**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
CRN (100986-85-4)

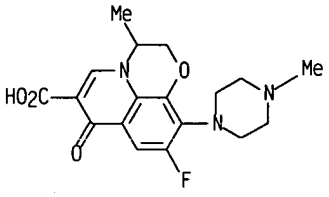
Absolute stereochemistry. Rotation (-).



x HBr

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 8 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **346587-03-9** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, ammonium salt (9CI) (CA INDEX NAME)
MF **C18 H20 F N3 O4 . H3 N**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
CRN (82419-36-1)



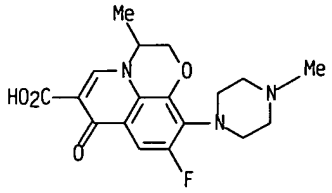
$\bullet NH_3$

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 9 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **346586-62-7** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, methanesulfonate (9CI) (CA INDEX NAME)
MF **C18 H20 F N3 O4 . x C H4 O3 S**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)

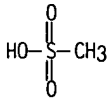
CM 1

CRN 82419-36-1
CMF C18 H20 F N3 O4



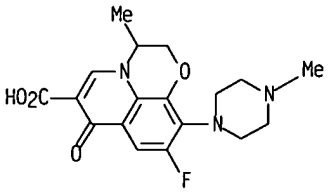
CM 2

CRN 75-75-2
CMF C H4 O3 S



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 10 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **346586-38-7** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,
9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-,
hydrobromide (9CI) (CA INDEX NAME)
MF **C18 H20 F N3 O4 . x Br H**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
CRN (82419-36-1)



● x HBr

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

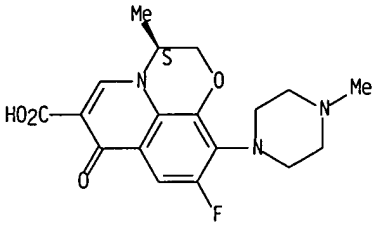
L13 ANSWER 11 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **226578-51-4** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,
9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-,
monomethanesulfonate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H20 F N3 O4 . C H4 O3 S**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Journal; Patent

RL.P Roles from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)

CM 1

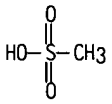
CRN 100986-85-4
CMF C18 H20 F N3 O4

Absolute stereochemistry. Rotation (-).



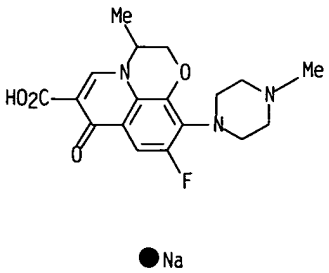
CM 2

CRN 75-75-2
CMF C H4 O3 S



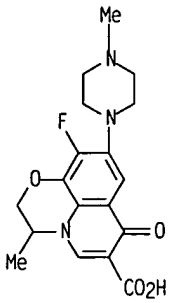
9 REFERENCES IN FILE CA (1907 TO DATE)
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 12 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **219522-15-3** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, sodium salt (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Ofloxacin sodium salt
MF **C18 H20 F N3 O4 . Na**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
CRN (82419-36-1)



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 13 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **197291-75-1** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,
10-fluoro-2,3-dihydro-3-methyl-9-(4-methyl-1-piperazinyl)-7-oxo- (9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF **C18 H20 F N3 O4**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: ANST (Analytical study)

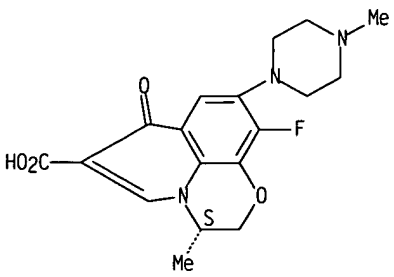


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 14 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **178912-62-4** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,
10-fluoro-2,3-dihydro-3-methyl-9-(4-methyl-1-piperazinyl)-7-oxo-, (S)-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H20 F N3 O4**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: ANST (Analytical study)

Absolute stereochemistry.

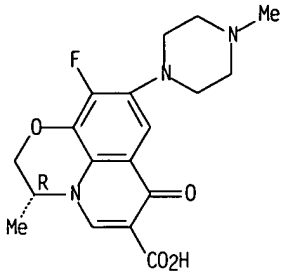


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 15 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **178912-61-3** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 10-fluoro-2,3-dihydro-3-methyl-9-(4-methyl-1-piperazinyl)-7-oxo-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H20 F N3 O4**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: ANST (Analytical study)

Absolute stereochemistry.

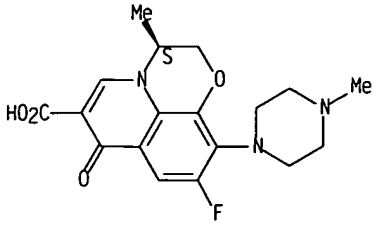



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 16 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **177325-13-2** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, monohydrochloride, (S)-
FS STEREOSEARCH
MF **C18 H20 F N3 O4 . Cl H**
SR CA
LC STN Files: CA, CAPLUS, CHEMCATS, IMSPATENTS, IMSRESEARCH, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PRP (Properties); USES (Uses)
CRN (100986-85-4)

Absolute stereochemistry. Rotation (-).

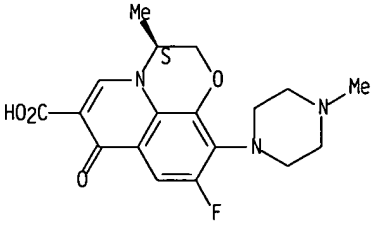


●HCl

8 REFERENCES IN FILE CA (1907 TO DATE)
8 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 17 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **138199-72-1** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, monohydrate, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H20 F N3 O4 . H2 O**
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, IMSPATENTS, IMSRESEARCH, IPA, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)
CRN (100986-85-4)

Absolute stereochemistry. Rotation (-).



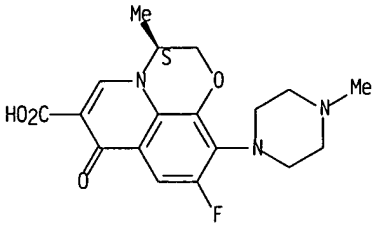
●H2O

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 18 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **138199-71-0** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, hydrate (2:1), (3S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, hydrate (2:1), (S)-
OTHER NAMES:

CN Levofloxacin hemihydrate
CN Levofloxacin hydrate
FS STEREOSEARCH
MF **C18 H20 F N3 O4 . 1/2 H2 O**
SR CA
LC STN Files: BEILSTEIN*, BIOTECHNO, CA, CAPLUS, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PHAR, PROUSDDR, PS, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PRP (Properties); USES (Uses)
CRN (100986-85-4)

Absolute stereochemistry. Rotation (-).



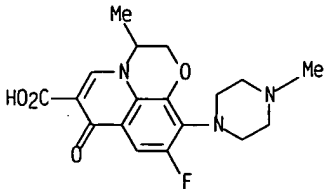

●1/2 $H_2O$

13 REFERENCES IN FILE CA (1907 TO DATE)
13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 19 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **134267-88-2** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, monoperchlorate, monohydrate (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (.+-.)-, monoperchlorate, monohydrate
OTHER NAMES:
CN Ofloxacin perchlorate monohydrate
MF **C18 H20 F N3 O4 . Cl H O4 . H2 O**
SR CA
LC STN Files: CA, CAPLUS, IMSPATENTS, IMSRESEARCH
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PRP (Properties)

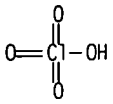
CM 1

CRN 82419-36-1
CMF C18 H20 F N3 O4



CM 2

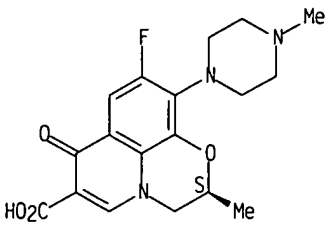
CRN 7601-90-3
CMF Cl H O4



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 20 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **129815-82-3** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-2-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H20 F N3 O4**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)

Absolute stereochemistry.



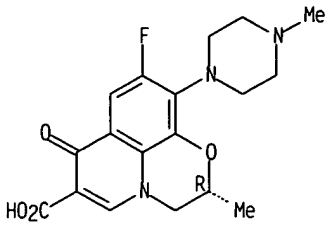
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 21 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **129798-62-5** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-2-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H20 F N3 O4**
SR CA

LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)

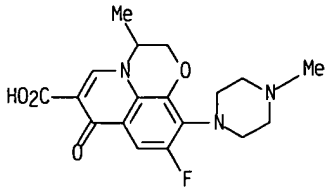
Absolute stereochemistry.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 22 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **118120-51-7** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, hydrochloride (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, hydrochloride, (.+-.)-
OTHER NAMES:
CN Ofloxacin hydrochloride
MF **C18 H20 F N3 O4 . x Cl H**
SR CA
LC STN Files: BIOSIS, CA, CAPLUS, CHEMCATS, IMSPATENTS, IMSRESEARCH, IPA, PS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PRP (Properties); USES (Uses)
CRN (82419-36-1)



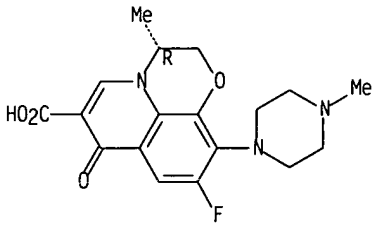

● x HCl

6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 23 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **100986-86-5** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,

9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3R)-
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,
9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (R)-
OTHER NAMES:
CN (+)-Ofloxacin
CN (R)-(+)-Ofloxacin
CN (R)-Ofloxacin
CN D-Ofloxacin
CN DR 3354
FS STEREOSEARCH
MF **C18 H20 F N3 O4**
SR CA
LC STN Files: ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CAPLUS, CASREACT, IMSPATENTS, IMSRESEARCH, IPA, PHAR, PROMT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study)

Absolute stereochemistry. Rotation (+).



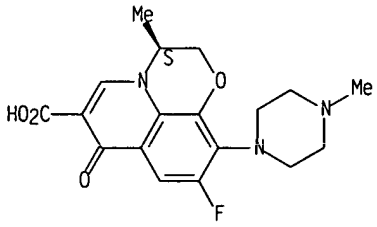

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

105 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
105 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 24 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **100986-85-4** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,
9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,
9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (S)-
OTHER NAMES:
CN (-)-Ofloxacin
CN (S)-(-)-Ofloxacin
CN (S)-Ofloxacin
CN Cravit
CN DR 3355
CN HR 355
CN Levaquin
CN Levofloxacin

CN Quixin
CN RWJ 25213-097
CN Tavanic
FS STEREOSEARCH
MF **C18 H20 F N3 O4**
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA CAplus document type: Book; Conference; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry. Rotation (-).

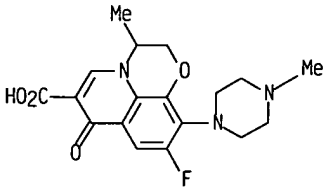



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

2186 REFERENCES IN FILE CA (1907 TO DATE)
18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2200 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L13 ANSWER 25 OF 25 REGISTRY COPYRIGHT 2005 ACS on STN
RN **82419-36-1** REGISTRY
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (.+-.)-
OTHER NAMES:
CN (.+-.)-Ofloxacin
CN 9-Fluoro-2,3-dihydro-3-methyl-10-(N-methylpiperazinyl)-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid
CN 9-Fluoro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid
CN DL 8280
CN Exocin
CN Flobacin

CN Floxal
CN Floxil
CN Floxin
CN HOE 280
CN Ocuflox
CN Oflocet
CN Oflocin
CN Oflox
CN Ofloxacin
CN Ofloxacine
CN ORF 18489
CN Oxaldin
CN PT 01
CN Tariferid
CN Tarivid
CN Visiren
CN Visren
FS 3D CONCORD
DR 85344-55-4, 83380-47-6, 86784-41-0, 303013-04-9
MF **C18 H20 F N3 O4**
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIUDB, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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40 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4126 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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=> => d ide l33

L33  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   75-05-8  REGISTRY
CN   Acetonitrile (8CI, 9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Acetonitrile cluster
CN   Cyanomethane
CN   Ethanenitrile
CN   Ethyl nitrile
CN   Methane, cyano-
CN   Methanecarbonitrile
CN   Methyl cyanide
CN   Methyl cyanide (MeCN)
CN   NSC 7593
FS   3D CONCORD
DR   54841-72-4
MF   C2 H3 N
CI   COM
LC   STN Files:   AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*,
       DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2,
       GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*,
       MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, PS, RTECS*,
       SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL, VTB
         (*File contains numerically searchable property data)
     Other Sources:   DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA  CAplus document type:  Book; Conference; Dissertation; Journal; Patent;
       Preprint; Report
RL.P   Roles from patents:  ANST (Analytical study); BIOL (Biological study);
       CMBI (Combinatorial study); FORM (Formation, nonpreparative); MSC
       (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process);
       PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role
       in record)
RLD.P  Roles for non-specific derivatives from patents:  ANST (Analytical
       study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP
       (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP  Roles from non-patents:  ANST (Analytical study); BIOL (Biological
       study); CMBI (Combinatorial study); FORM (Formation, nonpreparative);
       MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC
       (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses);
       NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents:  ANST (Analytical
       study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC
       (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process);
       PRP (Properties); RACT (Reactant or reagent); USES (Uses)


H3C-C≡N


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

          32782 REFERENCES IN FILE CA (1907 TO DATE)
            772 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          32859 REFERENCES IN FILE CAPLUS (1907 TO DATE)
             10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)


=> d his
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     (FILE 'HOME' ENTERED AT 10:06:58 ON 02 MAR 2005)

     FILE 'HCAPLUS' ENTERED AT 10:07:07 ON 02 MAR 2005
L1            1 US20040152701/PN
                E IN2002-MAS898/AP,PRN

     FILE 'REGISTRY' ENTERED AT 10:07:59 ON 02 MAR 2005

     FILE 'HCAPLUS' ENTERED AT 10:08:01 ON 02 MAR 2005
L2              TRA L1 1- RN :        3 TERMS

     FILE 'REGISTRY' ENTERED AT 10:08:01 ON 02 MAR 2005
L3            3 SEA L2

     FILE 'WPIX' ENTERED AT 10:08:06 ON 02 MAR 2005
L4            1 US20040152701/PN
                E IN2002-MAS898/AP,PRN

     FILE 'REGISTRY' ENTERED AT 10:14:04 ON 02 MAR 2005
L5          227 C18H20FN3O4
L6              QUE (PMS OR MAN OR IDS)/CI OR UNSPECIFIED OR COMPD OR COMPOUND
L7          212 L5 NOT L6
L8          141 L7 AND NR=4
L9          141 L8 NOT (MXS/CI OR MIXT)
L10          56 L9 AND NC2NC2/ES
L11           1 L10 AND L3
L12          34 NC2OC2-NC5-C6/ES AND L10
                SEL RN 1-2 6 8-14 16-26 28 30-31 34 L12
L13          25 E1-25 AND L12

     FILE 'HCAPLUS' ENTERED AT 10:24:03 ON 02 MAR 2005
L14        7023 L13 OR OFLOXACIN# OR LEVOFLOXACIN# OR DR3354 OR DR (1A) 3354 OR
L15          47 ORF18489 OR ORF (1A) 18 (1A) 489 OR OXALDIN OR PT01 OR PT (W) 0
L16         139 L14-15 (L) PREP+NT/RL
L17             QUE PY<=2002 OR AY<=2002 OR PRY<=2002
L18         129 L16 AND L17
                E REDDY M/AU
L19         129 E3,E112,E121-123
                E REDDY MANNE/AU
L20          29 E4-5
                E ESWARAIAH S/AU
L21          21 E3-4
                E REDDY K/AU
L22         248 E3,E106,E137
                E REDDY KOPPERA/AU
L23           1 E4
                E REDDY M/AU
L24          69 E3,E93
                E REDDY MARAM/AU
L25           1 E4
                E PRAKASH P/AU
L26          27 E3,E15
L27         204 (REDDY? (1A) LAB?)/CS,PA
L28           1 L16 AND L19-27
L29         128 L18 NOT L28
L30          76 L29 AND P/DT
L31          22 L30 AND US/PC
L32           2 L16 (L) CRYSTAL?

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                E ACETONITRILE/CN
L33           1 E3
L34        5853 C2H3N AND ACETONITRIL?
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L36      123334 L33 OR L35 OR ACETONITRILE OR CYANOMETHANE OR ETHANENITRILE OR
L37          10 L29 AND L36
                SEL AN 1-8 10 L37
L38           9 E1-18 AND L37
L39          11 L32 OR L38

=> b hcap
FILE 'HCAPLUS' ENTERED AT 10:54:20 ON 02 MAR 2005
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FILE COVERS 1907 - 2 Mar 2005  VOL 142 ISS 10
FILE LAST UPDATED: 1 Mar 2005  (20050301/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d al fhitstr 128 tot
'AL' IS NOT A VALID FORMAT FOR FILE 'HCAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
              SCAN must be entered on the same line as the DISPLAY,
              e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, IPC, and NCL

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels
```

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST; TI,IND; TI,SO. You may specify the format fields in any order and the information will be displayed in the same order as the format specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC to view a specified Accession Number.
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L28 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:633285 HCAPLUS
DN 141:162476
ED Entered STN: 06 Aug 2004
TI Novel anhydrous crystalline form of Levofloxacin and process for its preparation
IN **Reddy, Manne Satyanarayana; Eswaraiah, Sajja; Reddy, Koppera Ravinder; Reddy, Maram Reddy Sahadeva; Prakash, Pitta Jaya**
PA **Reddy's Laboratories** Limited, India; **Reddy's Laboratories**, Inc.
SO U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-58
ICS C07D491-02
NCL 514230500; 544105000
CC 63-8 (Pharmaceuticals)
Section cross-reference(s): 28
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI US 2004152701 | A1 | 20040805 | US 2003-716207 | 20031118 |
| PRAI IN 2002-MA898 | A | 20021202 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| US 2004152701 | ICM | A61K031-58 |

ICS C07D491-02
NCL 514230500; 544105000
US 2004152701 ECLA C07D498/04+265C+221C

AB A process for the preparation of an anhydrous crystalline form of an antimicrobial agent Levofloxacin comprises the condensation of N-methyl-piperazine with S(-)-9,10-difluoro-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de]-[1,4]-benzoxazine-6-carboxylic acid in acetonitrile followed by distillation of solvent to afford the residue, the resultant residue is refluxed with toluene and the solid is filtered at room temperature to afford the Levofloxacin. Levofloxacin was further refluxed in acetonitrile, filtered and dried to constant weight to give the anhydrous crystalline form of Levofloxacin. The anhydrous crystalline form of Levofloxacin is characterized by X-ray diffractogram, Differential Scanning Calorimetry thermogram and IR Spectra. 1.

ST levofloxacin anhyd cryst form prepn

IT **100986-85-4P, Levofloxacin**
RL: PRP (Properties); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of anhydrous crystalline form of **levofloxacin**)

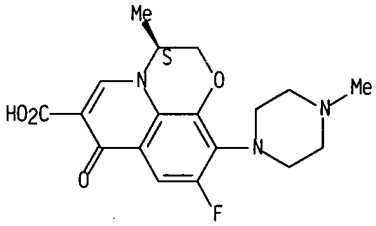
IT 109-01-3, N-Methylpiperazine 100986-89-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of anhydrous crystalline form of levofloxacin)

IT **100986-85-4P, Levofloxacin**
RL: PRP (Properties); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of anhydrous crystalline form of **levofloxacin**)

RN 100986-85-4 HCAPLUS

CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




=> d all hitstr l39 tot

L39 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:633285 HCAPLUS
DN 141:162476
ED Entered STN: 06 Aug 2004
TI Novel anhydrous crystalline form of Levofloxacin and process for its preparation
IN Reddy, Manne Satyanarayana; Eswaraiah, Sajja; Reddy, Koppera Ravinder; Reddy, Maram Reddy Sahadeva; Prakash, Pitta Jaya
PA Reddy's Laboratories Limited, India; Reddy's Laboratories, Inc.
SO U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-58
ICS C07D491-02
NCL 514230500; 544105000

CC 63-8 (Pharmaceuticals)
Section cross-reference(s): 28
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004152701 | A1 | 20040805 | US 2003-716207 | 20031118 |
| PRAI | IN 2002-MA898 | A | 20021202 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| US 2004152701 | ICM | A61K031-58 |
| | ICS | C07D491-02 |
| | NCL | 514230500; 544105000 |
| US 2004152701 | ECLA | C07D498/04+265C+221C |

AB A process for the preparation of an anhydrous crystalline form of an antimicrobial agent Levofloxacin comprises the condensation of N-methyl-piperazine with S(-)-9,10-difluoro-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de]-[1,4]-benzoxazine-6-carboxylic acid in acetonitrile followed by distillation of solvent to afford the residue, the resultant residue is refluxed with toluene and the solid is filtered at room temperature to afford the Levofloxacin. Levofloxacin was further refluxed in acetonitrile, filtered and dried to constant weight to give the anhydrous crystalline form of Levofloxacin. The anhydrous crystalline form of Levofloxacin is characterized by X-ray diffractogram, Differential Scanning Calorimetry thermogram and IR Spectra. 1.

ST levofloxacin anhyd cryst form prepn

IT **100986-85-4P, Levofloxacin**
RL: PRP (Properties); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of anhydrous **crystalline** form of **levofloxacin**)

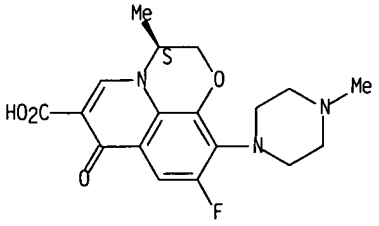
IT 109-01-3, N-Methylpiperazine 100986-89-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of anhydrous crystalline form of levofloxacin)

IT **100986-85-4P, Levofloxacin**
RL: PRP (Properties); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of anhydrous **crystalline** form of **levofloxacin**)

RN 100986-85-4 HCAPLUS

CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




L39 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN

AN **2003:590874** HCAPLUS

DN 139:154892

ED Entered STN: 01 Aug 2003

TI Methods for the purification of levofloxacin

IN Niddam-Hildesheim, Valerie; Gershon, Neomi; Schwartz, Eduard

PA Israel

SO U.S. Pat. Appl. Publ., 6 pp., Cont.-in-part of U.S. Ser. No. 262,965.

CODEN: USXXCO
DT Patent
LA English
IC ICM C07D043-04
NCL 544363000
CC 63-6 (Pharmaceuticals)
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2003144511 | A1 | 20030731 | US 2002-305180 | 20021127 <-- |
| PRAI | US 2001-326958P | P | 20011003 <-- | | |
| | US 2001-334316P | P | 20011129 <-- | | |
| | US 2002-354939P | P | 20020211 <-- | | |
| | US 2002-262965 | A2 | 20021003 <-- | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| US 2003144511 | ICM | C07D043-04 |
| | NCL | 544363000 |

AB Levofloxacin has been purified by dissolving levofloxacin in a polar solvent at an elevated temperature and crystallizing purified levofloxacin. Preferably, an antioxidant is added to increase the purity. Purified levofloxacin hemihydrate was obtained from a solution of crude levofloxacin in BuOH suspension.

ST levofloxacin purifn solvent crystn

IT Antioxidants
(addition prior to the crystallizing step in purification of levofloxacin)

IT Tocopherols
RL: MOA (Modifier or additive use); USES (Uses)
(addition prior to the crystallizing step in purification of levofloxacin)

IT Resins
RL: MOA (Modifier or additive use); USES (Uses)
(guaiacum; addition prior to the crystallizing step in purification of levofloxacin)

IT Crystallization
(polar solvents; purification of levofloxacin by dissolving levofloxacin in a polar solvent at an elevated temperature followed by crystallization)

IT Polar solvents
(purification of levofloxacin by dissolving levofloxacin in a polar solvent at an elevated temperature followed by crystallization)

IT 50-81-7, Ascorbic acid, uses 88-26-6, 4-Hydroxymethyl-2,6-di-tert-butylphenol 89-65-6, Erythorbic acid 111-17-1, Thiodipropionic acid 121-79-9, Propyl gallate 123-28-4, Dilauryl thiodipropionate 128-37-0, Butylated hydroxytoluene, uses 134-03-2, Sodium ascorbate 137-66-6, Ascorbic palmitate 1421-63-2, 2,4,5-Trihydroxybutyrophenone 1948-33-0, tert-Butylhydroquinone 5743-27-1, Calcium ascorbate 7681-57-4, Sodium metabisulfite 25013-16-5, Butylated hydroxyanisole
RL: MOA (Modifier or additive use); USES (Uses)
(addition prior to the crystallizing step in purification of levofloxacin)

IT 109-01-3, N-Methylpiperazine 100986-89-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and purification of levofloxacin)

IT **100986-85-4P, Levofloxacin 138199-71-0P, Levofloxacin** hemihydrate
RL: BSU (Biological study, unclassified); **PUR (Purification or recovery)**; **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(purification of **levofloxacin**)

IT 117678-38-3P, N-Oxide **levofloxacin** 117707-40-1P, Desmethyl **Levofloxacin**
RL: **BYP (Byproduct)**; **PREP (Preparation)**
(purification of **levofloxacin**)

IT 67-68-5, Dimethylsulfoxide, uses 71-36-3, Butanol, uses **75-05-8, Acetonitrile**, uses 78-93-3, Methyl ethyl ketone, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical

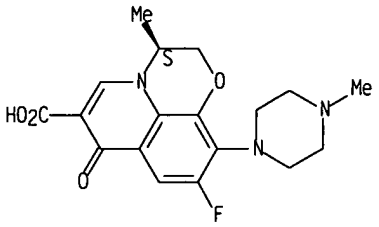
process); PYP (Physical process); PROC (Process); USES (Uses)
(solvent; purification of levofloxacin by dissolving levofloxacin in a polar solvent at an elevated temperature followed by crystallization)

IT 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)
(solvent; purification of levofloxacin by dissolving levofloxacin in **acetonitrile** and water at an elevated temperature followed by crystallization)

IT **100986-85-4P, Levofloxacin 138199-71-0P, Levofloxacin** hemihydrate
RL: BSU (Biological study, unclassified); **PUR (Purification or recovery)**; **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(purification of **levofloxacin**)

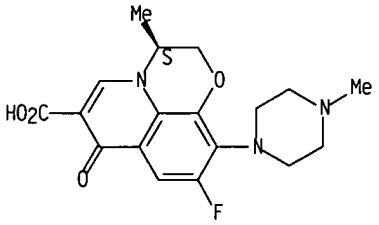
RN 100986-85-4 HCAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




RN 138199-71-0 HCAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, hydrate (2:1), (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




●1/2 $H_2O$

IT **75-05-8, Acetonitrile**, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)
(solvent; purification of levofloxacin by dissolving levofloxacin in a polar solvent at an elevated temperature followed by crystallization)

RN 75-05-8 HCAPLUS
CN Acetonitrile (8CI, 9CI) (CA INDEX NAME)

$H_3C-C\equiv N$

L39 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2003:434318** HCAPLUS
DN 139:12289
ED Entered STN: 06 Jun 2003
TI Methods for the purification of levofloxacin
IN Niddam-Hildesheim, Valerie; Gershon, Neomi; Schwartz, Eduard
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-6 (Pharmaceuticals)
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003045329 | A2 | 20030605 | WO 2002-US38182 | 20021127 <-- |
| | WO 2003045329 | A3 | 20040219 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 2003130507 | A1 | 20030710 | US 2002-263192 | 20021003 <-- |
| | EP 1460997 | A2 | 20040929 | EP 2002-791339 | 20021127 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| PRAI | US 2001-334316P | P | 20011129 <-- | | |
| | US 2002-354939P | P | 20020211 <-- | | |
| | US 2002-262965 | A2 | 20021003 <-- | | |
| | US 2002-263192 | A2 | 20021003 <-- | | |
| | US 2001-326958P | P | 20011003 <-- | | |
| | WO 2002-US38182 | W | 20021127 <-- | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2003045329 | ICM | A61K |

AB Levofloxacin has been purified by dissolving levofloxacin in a polar solvent at an elevated temperature and crystallizing purified levofloxacin. Preferably, an antioxidant is added to increase the purity. Purified levofloxacin hemihydrate was obtained from a solution of crude levofloxacin in BuOH suspension.

ST levofloxacin purifn solvent crystn
IT Resins
RL: MOA (Modifier or additive use); USES (Uses)
(guaiacum, antioxidant; purification of levofloxacin)
IT Antioxidants
Crystallization
(purification of levofloxacin)
IT 117678-38-3P
RL: **BYP (Byproduct)**; **PREP (Preparation)**
(antioxidant; purification of **levofloxacin**)
IT 50-81-7, Ascorbic acid, uses 88-26-6, 4-Hydroxymethyl-2,6-di-tert-butylphenol 89-65-6, Erythorbic acid 111-17-1, Thiodipropionic acid 121-79-9, Propyl gallate 123-28-4, Dilauryl thiodipropionate 128-37-0, Bht, uses 134-03-2, Sodium ascorbate 137-66-6, Ascorbic palmitate

1421-63-2, 2,4,5-Trihydroxybutyrophenone 1948-33-0, tert-Butylhydroquinone 5743-27-1, Calcium ascorbate 7681-57-4, Sodium metabisulfite 25013-16-5, Bha
RL: MOA (Modifier or additive use); USES (Uses)
(antioxidant; purification of levofloxacin)

IT 117707-40-1P
RL: **BYP (Byproduct)**; **PREP (Preparation)**
(purification of **levofloxacin**)

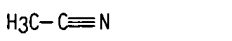
IT 67-68-5, Dmso, processes 71-36-3, 1-Butanol, processes **75-05-8**, **Acetonitrile**, processes 78-93-3, Mek, processes 7732-18-5, Water, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(purification of levofloxacin)

IT **100986-85-4P**, **Levofloxacin 138199-71-0P**, **Levofloxacin** hemihydrate
RL: **PUR (Purification or recovery)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(purification of **levofloxacin**)

IT 113400-30-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(purification of levofloxacin)

IT **75-05-8**, **Acetonitrile**, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(purification of levofloxacin)

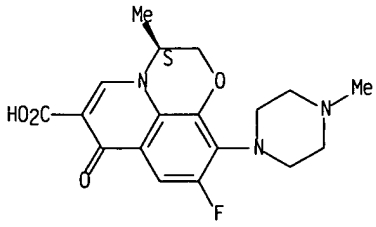
RN 75-05-8 HCAPLUS
CN Acetonitrile (8CI, 9CI) (CA INDEX NAME)



IT **100986-85-4P**, **Levofloxacin 138199-71-0P**, **Levofloxacin** hemihydrate
RL: **PUR (Purification or recovery)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(purification of **levofloxacin**)

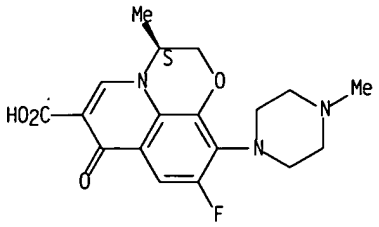
RN 100986-85-4 HCAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




RN 138199-71-0 HCAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, hydrate (2:1), (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



●1/2 $H_2O$

L39 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2003:282347** HCAPLUS
DN 138:292790
ED Entered STN: 11 Apr 2003
TI Methods for the purification of levofloxacin
IN Niddam-Hildesheim, Valerie; Gershon, Neomi; Schwartz, Eduard
PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-6 (Pharmaceuticals)
FAN.CNT 4

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003028665 | A2 | 20030410 | WO 2002-US31851 | 20021003 <-- |
| | WO 2003028665 | A3 | 20031120 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-326958P P 20011003 <--
US 2001-334316P P 20011129 <--
US 2002-354939P P 20020211 <--

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2003028665 | ICM | A61K |

AB Levofloxacin is purified by dissolving levofloxacin in a polar solvent at an elevated temperature and crystallizing purified levofloxacin. Preferably, an antioxidant is added to increase the purity. Crude levofloxacin 1.5 g and 36 mg ascorbic acid were put in suspension in 9.5 mL n-BuOH under inert atmospheric The mixture was heated to reflux temperature and a hot filtration was performed. The solution was then evaporated to dryness and n-BuOH (10 mL) was added. The mixture was heated to reflux until complete dissoln. and then cooled to RT over a period of 1.5 h. The precipitate was filtrated under vacuum, washed with n-BuOH and dried at 60.degree. in a vacuum oven to give 840 mg (56%) of purified levofloxacin hemihydrate.
ST levofloxacin purifn polar solvent
IT Resins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(guaiacum; methods for purification of levofloxacin)

IT Antioxidants
Crystallization
Polar solvents
(methods for purification of levofloxacin)

IT Tocopherols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for purification of levofloxacin)

IT 138199-71-0, Levofloxacin hemihydrate
RL: FMU (Formation, unclassified); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(methods for purification of levofloxacin)

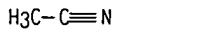
IT 67-68-5, Dimethyl sulfoxide, uses 71-36-3, Butanol, uses **75-05-8**, **Acetonitrile**, uses 78-93-3, Methyl ethyl ketone, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)
(methods for purification of levofloxacin)

IT **100986-85-4P, Levofloxacin**
RL: **PUR (Purification or recovery)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(methods for purification of **levofloxacin**)

IT 50-81-7, Ascorbic acid, biological studies 88-26-6, 4-Hydroxymethyl-2,6-di-tert-butylphenol 89-65-6, Erythorbic acid 111-17-1, Thiodipropionic acid 121-79-9, Propyl gallate 123-28-4, Dilauryl thiodipropionate 128-37-0, Butylated hydroxytoluene, biological studies 134-03-2, Sodium ascorbate 137-66-6, Ascorbic palmitate 1421-63-2, 2,4,5-Trihydroxybutyrophenone 1948-33-0, tert-Butylhydroquinone 5743-27-1, Calcium ascorbate 7681-57-4, Sodium metabisulfite 25013-16-5, Butylated hydroxyanisole
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for purification of levofloxacin)

IT **75-05-8, Acetonitrile**, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)
(methods for purification of levofloxacin)

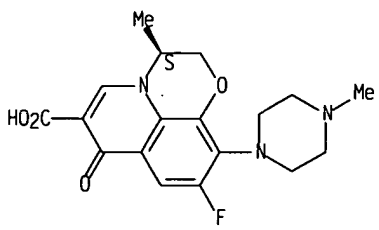
RN 75-05-8 HCAPLUS
CN Acetonitrile (8CI, 9CI) (CA INDEX NAME)



IT **100986-85-4P, Levofloxacin**
RL: **PUR (Purification or recovery)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(methods for purification of **levofloxacin**)

RN 100986-85-4 HCAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L39 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:859275 HCAPLUS
DN 139:73856
ED Entered STN: 13 Nov 2002
TI Complexes of Co(II) and Zn(II) with ofloxacin. Crystal structure of [Co(oflo)2(MeOH)2].cntdot.4MeOH
AU Macias, Benigno; Villa, Maria V.; Sastre, Maria; Castineiras, Alfonso; Borras, Joaquin
CS Departamento de Quimica Inorganica, Facultad de Farmacia, Universidad de Salamanca, Spain
SO Journal of Pharmaceutical Sciences (2002), 91(11), 2416-2423
CODEN: JPMSAE; ISSN: 0022-3549
PB Wiley-Liss, Inc.
DT Journal
LA English
CC 63-5 (Pharmaceuticals)
AB Ofloxacin (oflo) is able to interact with Co(II) and Zn(II) salts to form complexes with the general formula [M(oflo)2].cntdot.4H2O, (M = Co, Zn). Bonding takes place through one of the oxygen atoms of the carboxylate group (acting as a monodentate) and the oxygen atom of the ketonic group. The IR bands of the carboxylic and ketonic group at 1713 and 1622 cm-1, resp., shift to 1615 and 1575 cm-1 in the complexes. After dissoln. in methanol, complex [Co(oflo)2].cntdot.4H2O crystallizes as [Co(oflo)2(MeOH)2].cntdot.4MeOH, where Co(II) ion is in an octahedral environment of oxygen atoms. This compound crystallizes in the triclinic system, spatial group P-1, with unit cell dimensions a = 9.3670(12), b = 11.4135(17), c = 11.851(2) .ANG., y .alpha. = 71.999(14), .beta. = 73.698(12), .gamma. = 83.528(14).degree.. Magnetic properties (effective magnetic moment 5.02 BM) and visible spectrum (bands at 490, 510, and 1152 nm) are characteristic of such an octahedral geometry. 1H- and 13C-NMR spectra of the Zn(II) complex indicate only small structural changes in ofloxacin upon coordination to the metallic site.
ST ofloxacin cobalt zinc complex methanol crystn
IT NMR (nuclear magnetic resonance)
(carbon-13; of ofloxacin Co(II) and Zn(II) complexes)
IT Crystal structure
IR spectra
Mass spectra
NMR (nuclear magnetic resonance)
(of ofloxacin Co(II) and Zn(II) complexes)
IT 82419-36-1D, Ofloxacin., complexes
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Co(II) and Zn(II) complexes of ofloxacin)
IT 550358-69-5P
RL: PRP (Properties); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(**crystal** structure; of **ofloxacin** Co(II) and Zn(II) complexes)
IT 439086-11-0 550358-67-3
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of ofloxacin Co(II) and Zn(II) complexes)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; International tables for X-ray crystallography 1995, V100
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data 1997
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(8) Macias, B; Int J Pharm 1994, V106, P229
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(11) Nonius, B; CAD4-express software Ver 5.1/1.2 1994
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(14) Ruiz, M; Inorg Chim Acta 1993, V211, P133 HCAPLUS
(15) Ruiz, M; Inorg Chim Acta 1994, V217, P149 HCAPLUS
(16) Ruiz, M; J Inorg Biochem 1988, V69, P231
(17) Ruiz, M; J Inorg Biochem 1995, V59, P801 HCAPLUS
(18) Ruiz, M; J Inorg Biochem 1997, V65, P87 HCAPLUS
(19) Sheldrick, G; Acta Crystallogr 1990, VA46, P467 HCAPLUS
(20) Sheldrick, G; SHELXL-97 Program for the refinement of crystal structures 1997
(21) Sigel, H; Metal ions in biological systems 1985, V19
(22) Spek, A; PLATON A multipurpose crystallographic tool 2000
(23) Wolfson, J; Quinolone antimicrobial agents 1989

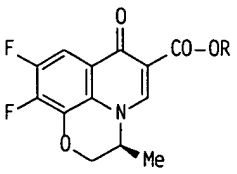
L39 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2001:463228** HCAPLUS
DN 135:61344
ED Entered STN: 27 Jun 2001
TI Process for the preparation of pyridobenzoxazine derivatives
IN Noguchi, Shigeru; Yokoyama, Yukio
PA Daiichi Seiyaku Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07D498-06
ICS B01J031-26; C07B061-00
CC 28-13 (Heterocyclic Compounds (More Than One Hetero Atom))
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI JP 2001172283 | A2 | 20010626 | JP 1999-355916 | 19991215 <-- |
| PRAI JP 1999-355916 | | 19991215 <-- | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| JP 2001172283 | ICM | C07D498-06 |
| | ICS | B01J031-26; C07B061-00 |

OS CASREACT 135:61344; MARPAT 135:61344
GI




I

AB The title compds. I [R = alkyl, etc.], useful as intermediates for levofloxacin, are prepared in several steps from 2,3,4,5-tetrafluorobenzoyl chloride (II). Thus, a mixture of II and Et2NCH:CHCO2Et in o-xylene containing triethylamine was stirred for 1 h at 50.degree.; L-alaninol was then added, and the resulting mixture was stirred for a further 1 h; potassium

carbonate, tetrabutylammonium bromide and o-xylene were then added to the reaction mixture; the resulting mixture was refluxed for 3 h to give I [R = ethyl] in 54.1% yield.

ST pyridobenzoxazinecarboxylate prepn levofloxacin intermediate; levofloxacin intermediate pyridobenzoxazinecarboxylate prepn

IT Cyclization
(cyclization of tetrafluorobenzoylhydroxypropylaminoacrylate)

IT Carbonates, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(metal; process for preparation of pyridobenzoxazine derivs. as intermediates for levofloxacin)

IT Phase transfer catalysts
(process for preparation of pyridobenzoxazine derivs. as intermediates for levofloxacin)

IT Aromatic hydrocarbons, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; process for preparation of pyridobenzoxazine derivs. as intermediates for levofloxacin)

IT Substitution reaction
(substitution reaction of tetrafluorobenzoyl chloride with alkyl dialkylaminoacrylate)

IT 56-37-1, Benzyltriethylammonium chloride 1643-19-2, Tetrabutylammonium bromide 5922-92-9, Tetrahexylammonium chloride 17455-13-9, 18-crown-6 25316-59-0, Benzyltributylammonium bromide
RL: CAT (Catalyst use); USES (Uses)
(phase transfer catalyst; process for preparation of pyridobenzoxazine derivs. as intermediates for levofloxacin)

IT 110548-02-2P 345317-64-8P
RL: **IMF (Industrial manufacture)**; RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(process for preparation of pyridobenzoxazine derivs. as intermediates for **levofloxacin**)

IT 106939-34-8P
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(process for preparation of pyridobenzoxazine derivs. as intermediates for **levofloxacin**)

IT 100986-85-4, Levofloxacin
RL: MSC (Miscellaneous)
(process for preparation of pyridobenzoxazine derivs. as intermediates for levofloxacin)

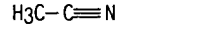
IT 584-08-7, Potassium carbonate 2749-11-3, L-Alaninol 3001-72-7, DBN 6674-22-2, DBU 36149-51-6 94695-48-4, 2,3,4,5-Tetrafluorobenzoyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of pyridobenzoxazine derivs. as intermediates for levofloxacin)

IT 71-43-2, Benzene, uses **75-05-8**, **Acetonitrile**, uses 95-47-6, o-Xylene, uses 108-88-3, Toluene, uses 1330-20-7, Xylene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; process for preparation of pyridobenzoxazine derivs. as intermediates for levofloxacin)

IT **75-05-8**, **Acetonitrile**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; process for preparation of pyridobenzoxazine derivs. as intermediates for levofloxacin)

RN 75-05-8 HCAPLUS

CN Acetonitrile (8CI, 9CI) (CA INDEX NAME)



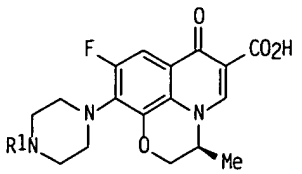
L39 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **2000:608752** HCAPLUS
DN 133:193174
ED Entered STN: 01 Sep 2000
TI Preparation of (-)-pyridobenzoxazinecarboxylates from (+)-ethyl 2-(4-chloro-5-fluoro-2-halo-3-nitobenzoyl)-3-[(1-hydroxypropy-2(S)-yl)amino]acrylate.
IN Park, Young-jun; Lee, Ho-seong; Kim, Min-hwan; Kim, Kyung-chul
PA Samsung Electronics Co., Ltd., S. Korea
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D498-06
ICS C07D265-38; C07D241-04
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2000050428 | A1 | 20000831 | WO 2000-KR145 | 20000223 <-- |
| | W: BR, CN, IN, US | | | | |
| | RW: DE, ES, FR, GB, IT | | | | |
| | KR 2000056615 | A | 20000915 | KR 1999-6093 | 19990224 <-- |
| | JP 2000247980 | A2 | 20000912 | JP 1999-228868 | 19990812 <-- |
| | JP 3530784 | B2 | 20040524 | | |
| | BR 2000005132 | A | 20010102 | BR 2000-5132 | 20000223 <-- |
| | EP 1073662 | A1 | 20010207 | EP 2000-905443 | 20000223 <-- |
| | EP 1073662 | B1 | 20040414 | | |
| | R: DE, ES, FR, GB, IT | | | | |
| | CN 1125073 | B | 20031022 | CN 2000-800214 | 20000223 <-- |
| | ES 2215024 | T3 | 20041001 | ES 2000-905443 | 20000223 <-- |
| | JP 2000299412 | A2 | 20001024 | JP 2000-47715 | 20000224 <-- |
| | US 6316618 | B1 | 20011113 | US 2000-674323 | 20001024 <-- |
| PRAI | KR 1999-6093 | A | 19990224 <-- | | |
| | WO 2000-KR145 | W | 20000223 <-- | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2000050428 | ICM | C07D498-06 |
| | ICS | C07D265-38; C07D241-04 |
| US 6316618 | ECLA | C07D215/56B; C07D498/06+265C+221C <-- |

OS CASREACT 133:193174; MARPAT 133:193174
GI



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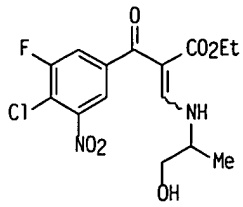

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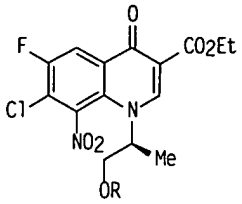


III

AB Title compds. (I; R1 = H, alkyl) were prepared by (1) reaction of aminoacrylates (II; X = halo; R = H) with RaZ [Ra = COR2; R2 = alkyl, alkoxy, cycloalkoxy, (substituted) Ph, etc.; Z = leaving group] or RbNCY [Rb = alkyl, (substituted) Ph] to give II [X = halo; R = COR2, RbNHCY; R2 = alkyl, alkoxy, cycloalkoxy, (substituted) Ph, etc.; Rb = alkyl, (substituted) Ph; Y = O, S], (2) treatment of the latter with base in an organic polar solvent to give III (R as above), (3) treatment of III with (R1-substituted) piperazine in an organic polar solvent in the presence of base, and (4) hydrolysis and cyclization in the presence of metal hydroxide in an organic solvent. Thus, (+)-Et 2-(2,4-dichloro-3-nitro-5-fluorobenzoyl)-3-[(1-hydroxyprop-2(S)-yl)amino]acrylate in ethylene dichloride at -40.degree. was treated with Et3N and AcCl to give 100% (+)-Et 2-(2,4-dichloro-3-nitro-5-fluorobenzoyl)-3-[(1-acetoxypropyl-2(S)-yl)amino]acrylate. The latter was refluxed with K2CO3 in **MeCN** to give 96% (-)-Et N-(1-acetoxyprop-2(S)-yl)-6-fluoro-7-chloro-8-nitro-4-quinolone-3-carboxylate. This was refluxed with N-methylpiperazine and K2CO3 in **MeCN** to give 100% (-)-Et N-(1-acetoxyprop-2(S)-yl)-6-fluoro-7-(N-methylpiperazinyl)-8-nitro-4-quinolone-3-carboxylate. The latter was refluxed with KOH in EtOH to give 57% I (R1 = Me).

ST pyridobenzoxazinecarboxylate prepn; chlorofluorohalonitobenzoylhydroxyprop ylaminoacryate acylation amination cyclization

IT **100986-85-4P**
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of (-)-pyridobenzoxazinecarboxylates from (+)-Et 2-(4-chloro-5-fluoro-2-halo-3-nitobenzoyl)-3-[(1-hydroxypropy-2(S)-yl)amino]acrylate)

IT 109-01-3, N-Methylpiperazine 289688-82-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (-)-pyridobenzoxazinecarboxylates from (+)-Et 2-(4-chloro-5-fluoro-2-halo-3-nitobenzoyl)-3-[(1-hydroxypropy-2(S)-yl)amino]acrylate)

IT 289688-76-2P 289688-77-3P 289688-78-4P 289688-79-5P 289688-80-8P 289688-81-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (-)-pyridobenzoxazinecarboxylates from (+)-Et 2-(4-chloro-5-fluoro-2-halo-3-nitobenzoyl)-3-[(1-hydroxypropy-2(S)-yl)amino]acrylate)

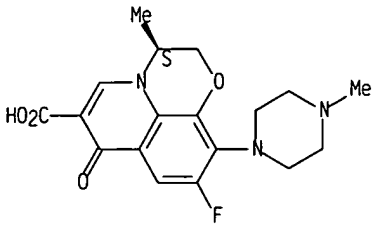
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Abbott Laboratories; US 477273 1988
(2) Daiichi Seiyaku Co; JP 01165589 A 1989 HCAPLUS

(3) The Upjohn Company; WO 9012799 A1 1990 HCAPLUS
IT **100986-85-4P**
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of (-)-pyridobenzoxazinecarboxylates from (+)-Et 2-(4-chloro-5-fluoro-2-halo-3-nitobenzoyl)-3-[(1-hydroxypropy-2(S)-yl)amino]acrylate)
RN 100986-85-4 HCAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)- (9CI) (CA INDEX NAME)

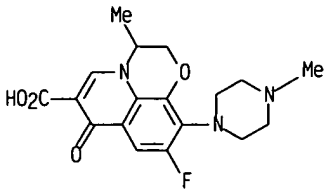
Absolute stereochemistry. Rotation (-).




L39 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1997:780313** HCAPLUS
DN 128:119535
ED Entered STN: 13 Dec 1997
TI Spectrofluorimetric study of the acid-base equilibria and complexation behavior of the fluoroquinolone antibiotics ofloxacin, norfloxacin, ciprofloxacin and pefloxacin in aqueous solution
AU Drakopoulos, Anargiros I.; Ioannou, Pinelopi C.
CS Panepistimiopolis, University of Athens, Laboratory of Analytical Chemistry, 15771 Athens, Greece
SO Analytica Chimica Acta (**1997**), 354(1-3), 197-204
CODEN: ACACAM; ISSN: 0003-2670
PB Elsevier Science B.V.
DT Journal
LA English
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1, 64, 68, 80
AB A spectrofluorimetric study of the acid-base properties and of the complexation behavior of the fluoroquinolone antibiotics ofloxacin (OF), norfloxacin (NOR), ciprofloxacin (CIP) and pefloxacin (PEF) was performed. Their dissociation consts. were determined by a combined potentiometric/fluorimetric technique. All studied fluoroquinolones form fluorescent complexes with Sc3+ in slightly acidic solns. [pH 4.2, .lambda.ex 280 nm, .lambda.em 430 nm (480 nm for OF)]. A simple, rapid and sensitive spectrofluorimetric method based on the formation of scandium complexes was developed for the determination of OF, NOR, CIP and PEF in aqueous solns. Calibration graphs for all 4 fluoroquinolones were linear up to 1.0 .mu.M, with results having a mean relative error of 3.2. The 3.sigma. detection limits were 1.1, 0.6, 0.5 and 1.0 nM for OF, NOR, CIP and PEF, resp. The method was successfully applied to the determination of NOR in synthetic serum samples (5.0-50.0 .mu.M) after deproteination with **MeCN** [serum-**MeCN** (1:2)] with a mean recovery of 93.4%.
ST spectrofluorimetry fluoroquinolone antibiotic complex metal detn; acid base equil fluoroquinolone antibiotic
IT Acid-base equilibrium
Blood analysis
Dissociation constant
Fluorometry
Pharmaceutical analysis

Potentiometry
Protonation
(spectrofluorimetric study of acid-base equilibrium and complexation of fluoroquinolone antibiotics in solution)
IT 13721-01-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(derivs., antibiotics: spectrofluorimetric study of acid-base equilibrium and complexation of fluoroquinolone antibiotics in solution)
IT 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 82419-36-1, Ofloxacin 85721-33-1, Ciprofloxacin
RL: ANT (Analyte); PRP (Properties); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(spectrofluorimetric study of acid-base equilibrium and complexation of fluoroquinolone antibiotics in solution)
IT 7429-90-5, Aluminum, reactions 7440-20-2, Scandium, reactions
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(spectrofluorimetric study of acid-base equilibrium and complexation of fluoroquinolone antibiotics in solution)
IT 151-21-3, Sodium dodecyl sulfate, uses
RL: NUU (Other use, unclassified); USES (Uses)
(spectrofluorimetric study of acid-base equilibrium and complexation of fluoroquinolone antibiotics in solution)
IT 7429-90-5DP, Aluminum, fluoroquinolone antibiotic complexes, preparation
7440-20-2DP, Scandium, fluoroquinolone antibiotic complexes, preparation
70458-92-3DP, Pefloxacin, metal complexes 70458-96-7DP, Norfloxacin, metal complexes **82419-36-1DP, Ofloxacin**, metal complexes 85721-33-1DP, Ciprofloxacin, metal complexes
RL: PRP (Properties); **SPN (Synthetic preparation)**; **PREP (Preparation)**
(spectrofluorimetric study of acid-base equilibrium and complexation of fluoroquinolone antibiotics in solution)
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bridges, J; Biochem J 1966, V98, P401
(2) Byungse, S; Med Clin North America 1995, V79, P869
(3) Clement, J; Antimicrob Agents and Chemother 1994, V38, P1071 HCAPLUS
(4) Cook, P; J Antimicrob Chemother 1995, V35, P317 HCAPLUS
(5) Djurdjevic, P; Anal Chim Acta 1995, V300, P253 HCAPLUS
(6) Ioannou, P; Talanta 1987, V34, P857 HCAPLUS
(7) Issopoulos, P; Analyst 1989, V114, P627 HCAPLUS
(8) Kitzes-Chohen, R; Quionolone Bull 1987, V3, P7
(9) Lecomte, S; Antimicrob Agents and Chemother 1994, V38, P2810 HCAPLUS
(10) Lee, D; J Pharm and Biomed Analysis 1994, V12, P157 HCAPLUS
(11) Lianidou, E; Anal Chim Acta 1996, V320, P107 HCAPLUS
(12) Martinez-Cabarga, M; Antimicrob Agents Chemother 1991, V35, P2102 HCAPLUS
(13) Maxwell, A; J Antimicrob Chemother 1992, V30, P409 HCAPLUS
(14) Okabayashi, Y; Chem Pharm Bull 1992, V40, P692 HCAPLUS
(15) Palu, G; Proc Natl Acad Sci USA 1992, V89, P9671 HCAPLUS
(16) Panadero, S; Anal Chim Acta 1995, V303, P39 HCAPLUS
(17) Ross, D; Int J Pharm 1990, V63, P237 HCAPLUS
(18) Ross, D; J Pharm and Biomed Analysis 1994, V12, P1325 HCAPLUS
(19) Shen, L; Biochemistry 1989, V28, P3886 HCAPLUS
(20) Stein, G; Am J Med 1987, V82, P18 HCAPLUS
(21) Takacs-Novak, K; J Pharm Sci 1990, V79, P1023 HCAPLUS
(22) Veiopoulou, C; J Pharm and Biomed Analysis, in press 1996
(23) Willmott, C; J Mol Biol 1994, V242, P351 HCAPLUS
(24) Yu, X; Pharm Res 1994, V11, P522 HCAPLUS
IT **82419-36-1DP, Ofloxacin**, metal complexes
RL: PRP (Properties); **SPN (Synthetic preparation)**; **PREP (Preparation)**
(spectrofluorimetric study of acid-base equilibrium and complexation of fluoroquinolone antibiotics in solution)

RN 82419-36-1 HCAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo- (9CI) (CA INDEX NAME)




L39 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1996:596081** HCAPLUS
DN 125:247630
ED Entered STN: 07 Oct 1996
TI Trimethylsilyl esters and solvates of chelates of quinoline-3-carboxylic acids, and their preparation and use in a process for quinolone antibacterials.
IN Palomo Nicolau, Francisco Eugenio; Solis Oller, Jose Maria; Palomo Coll, Antonio Luis
PA Centro Marga Para La Investigacion S.A., Spain
SO Span., 14 pp.
CODEN: SPXXAD
DT Patent
LA Spanish
IC ICM C07D215-56
ICS C07F005-02; C07F005-06
CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 29, 45
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | ES 2077490 | A1 | 19951116 | ES 1992-2560 | 19921118 <-- |
| | ES 2077490 | B1 | 19961016 | | |
| PRAI | ES 1992-2560 | | 19921118 <-- | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| ES 2077490 | ICM | C07D215-56 |
| | ICS | C07F005-02; C07F005-06 |

OS CASREACT 125:247630; MARPAT 125:247630
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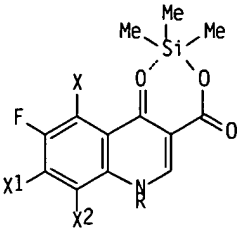

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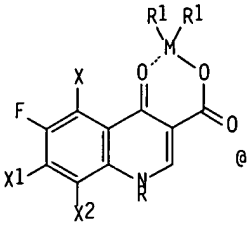

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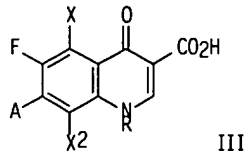


III

AB Trimethylsilyl esters I and chelates II [X = H, NH2, NHAc, Me; X1 = halo, alkylsulfonyl, arylsulfonyloxy; X2 = H, halo, Me, OMe, OCHF2, OH, SO3H, NO2; when X = H, then X1 and X2 do not both = F; R = alkyl, cycloalkyl, alkylamino, aryl, alkylarom. group; X2R may form 5- or 6-membered heterocycle; M = B, Al; R1 = halo, acyloxy; n = 0.5-2.0] are claimed. The compds. are intermediates for quinolone antibacterials III [A = substituted amino]. For instance, 1-cyclopropyl-7-chloro-1,4-dihydro-6-fluoro-4-oxo-3-quinolinecarboxylic acid reacted with HN(SiMe3)2 in refluxing CHCl3 to give 99% I [X = X2 = H; X1 = Cl; R = cyclopropyl]. This reacted with BF3 in **MeCN**/1,4-dioxane mixture at 12-15.degree. and then 20-25.degree. to give II [M = B; R1 = F; n unspecified; others as above] in virtually quant. yield. Reaction of this with anhydrous piperazine in DMSO at 50-65.degree., followed by hydrolysis with 10% NaOH at 60.degree., gave the corresponding III [A = piperazino], i.e. ciprofloxacin.

ST quinolinecarboxylate trimethylsilyl boron chelate prepn intermediate; quinolone antibacterial intermediate prepn

IT Bactericides, Disinfectants, and Antiseptics
(preparation of quinolinecarboxylic acid trimethylsilyl esters and chelate solvates as intermediates for quinolones)

IT 68077-26-9DP, 1-Ethyl-7-chloro-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid, boron complexes 75338-42-0DP, 1-Ethyl-6,7,8-trifluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid, boron complexes 82419-35-0DP, 9,10-Difluoro-2,3-dihydro-3-methyl-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, boron complexes 87531-64-4P 93107-30-3DP, boron complexes 94695-52-0DP, 1-Cyclopropyl-6,7,8-trifluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid, boron complexes 98105-93-2DP, 1-(2,4-Difluorophenyl)-7-chloro-6-fluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid, boron complexes **100986-85-4DP**, boron complexes 101987-89-7DP, boron complexes 103772-14-1DP, 5-Amino-1-cyclopropyl-6,7,8-trifluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid, boron complexes 111764-60-4P 111764-62-6P 122050-30-0P 126362-87-6DP, boron complexes 128426-95-9DP, boron complexes 128427-03-2DP, boron complexes 140412-78-8DP, boron complexes 181576-10-3P 181576-12-5P 181576-13-6P 181576-14-7P 181576-15-8P 181576-16-9P 181576-17-0P 181576-18-1P 181576-19-2P 181576-20-5P 181576-21-6P 181576-22-7P 181576-23-8P 181576-24-9DP, boron complexes 181576-25-0P 181576-26-1P
RL: **IMF (Industrial manufacture)**; RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; preparation of quinolinecarboxylic acid trimethylsilyl esters

and chelate solvates as intermediates for quinolones)

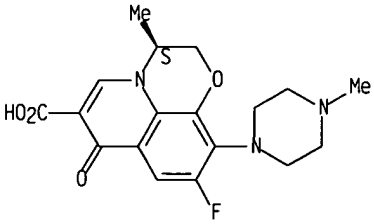
IT 7429-90-5DP, Aluminum, complexes with oxoquinolinecarboxylic acids
7440-42-8DP, Boron, complexes with oxoquinolinecarboxylic acids
70458-92-3P **82419-36-1P** 85721-33-1P 91188-00-0P,
1-Ethyl-7-[3-[(ethylamino)methyl]-1-pyrrolidinyl]-6,8-difluoro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid 93106-60-6P 93107-08-5P 98079-52-8P
99735-00-9P 100936-45-6P 100936-51-4P **100986-85-4P**
105956-97-6P 107480-49-9P 110871-86-8P 111810-64-1P 181576-29-4P
181576-30-7P
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of quinolinecarboxylic acid trimethylsilyl esters and chelate solvates as intermediates for quinolones)

IT 109-01-3, N-Methylpiperazine 110-85-0, Piperazine, reactions 658-24-2,
2,5-Diazabicyclo[2.2.2]octane 672-28-6, 2,5-Diazabicyclo[2.2.1]heptane
5167-08-8, 1,4-Diazabicyclo[3.2.1]octane 5308-25-8, N-Ethylpiperazine
40499-83-0, 3-Hydroxypyrrolidine 75338-42-0, 1-Ethyl-6,7,8-trifluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid 82419-35-0,
9,10-Difluoro-2,3-dihydro-3-methyl-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid 83030-08-4, 3-(Methylamino)pyrrolidine
84922-95-2, exo-3-Amino-8-azabicyclo[3.2.1]octane 86393-33-1
91187-83-6, 3-[(Ethylamino)methyl]pyrrolidine 94695-52-0,
1-Cyclopropyl-6,7,8-trifluoro-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid
100944-14-7, 2,5-Diazabicyclo[2.2.1]heptane dihydrobromide 100986-89-8
110842-64-3, 1-Acetyl-2-methylpiperazine 181576-27-2,
1-Acetyl-2,6-dimethylpiperazine 181576-28-3, 3-[(Acetylamino)methyl]pyrrolidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of quinolinecarboxylic acid trimethylsilyl esters and chelate solvates as intermediates for quinolones)

IT **100986-85-4DP**, boron complexes
RL: **IMF (Industrial manufacture)**; RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; preparation of quinolinecarboxylic acid trimethylsilyl esters and chelate solvates as intermediates for quinolones)

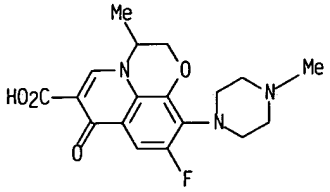
RN 100986-85-4 HCAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



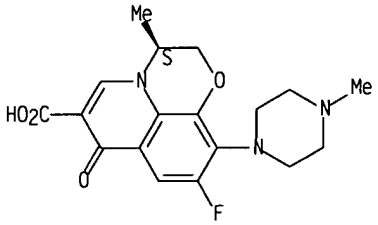

IT **82419-36-1P 100986-85-4P**
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of quinolinecarboxylic acid trimethylsilyl esters and chelate solvates as intermediates for quinolones)

RN 82419-36-1 HCAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo- (9CI) (CA INDEX NAME)



RN 100986-85-4 HCAPLUS
CN 7H-Pyrido[1.2.3-de]-1.4-benzoxazine-6-carboxylic acid.
9-fluoro-2.3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-. (3S)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



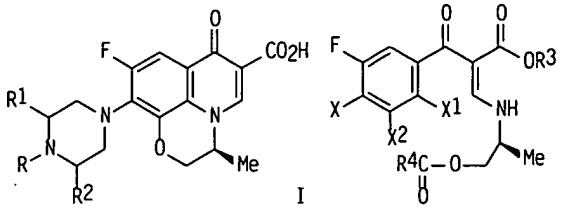
L39 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1996:494614** HCAPLUS
DN 125:195666
ED Entered STN: 20 Aug 1996
TI Method for the preparation of bactericidal (-)
piperazinylpyridobenzoxazine derivatives via cyclization of a
2-aminomethylene-3-oxo-3-phenylpropionate intermediate
IN Kim. Youseung; Kang. Soon Bang; Park. Seonhee
PA Korea Institute of Science and Technology. S. Korea
SO U.S.. 8 pp.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07D498-06
NCL 544101000
CC 28-13 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 63
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 5539110 | A | 19960723 | US 1994-321360 | 19941011 <-- |
| | KR 125115 | B1 | 19971205 | KR 1994-5762 | 19940322 <-- |
| PRAI | KR 1994-5762 | A | 19940322 <-- | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| US 5539110 | ICM | C07D498-06 |
| | NCL | 544101000 |

OS CASREACT 125:195666; MARPAT 125:195666
GI




AB A method is claimed for the preparation of (-) piperazine benzoxazine derivative I wherein R, R1 and R2 each is a hydrogen or a C1-C4 alkyl group, comprising the steps of: reacting (+)-2-aminomethylene-3-oxo-3-phenylpropionate derivative II wherein R3 and R4 each is a C1-C4 alkyl group, and X and X1 each is a halogen or nitro group, and X2 is a halogen, with a base in an organic polar solvent, to give a (-) benzoxazine derivative III wherein X is defined as above; and reacting III with a piperazine derivative IV wherein R, R1 and R2 are defined as above, and Z is a hydrogen or trialkylsilyl group which alkyl is a C1-C4 alkyl group, in an organic polar solvent. Thus, addition reaction of (+)-2-amino-1-propanol with Et propiolate afforded Z/E Et 3-[(1-hydroxyprop-2(S) -yl)amino]acrylate (99%) which was acetylated to Z/E Et 3-[(1-acetoxyprop-2(S)-yl)amino]acrylate (98%); acylation of the latter with 2,3,4,5-tetrafluorobenzoyl chloride afforded Z/E Et 2-(2,3,4,5-tetrafluorobenzoyl)-3-[[1-acetoxyprop-2(S)-yl]amino]acrylate (II; R4 = Me, R3 = Et; X, X1, X2 = F; 97%); treatment of the latter with KOH/THF afforded (-)-9,10-difluoro-2,3-dihydro-3(S)-methyl-7-oxo-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid (III; X = F, 81%); substitution of the latter with N-methylpiperazine afforded 91% (-)-9-fluoro-3(S)-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-2,3-dihydro-7H-pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid (I; R = Me, R1 = R2 = H).

ST bactericidal piperazinyl pyridobenzoxazine deriv prepn; benzoxazine pyrido piperazinyl bactericidal prepn; cyclization aminomethyleneoxophenylpropionate

IT Ring closure and formation
(preparation of bactericidal (-) piperazinylpyridobenzoxazine derivs. via cyclization of a 2-aminomethylene-3-oxo-3-phenylpropionate intermediate)

IT 497-19-8, Sodium carbonate, reactions 513-77-9, Barium carbonate 554-13-2, Lithium carbonate 584-08-7, Potassium carbonate 1305-62-0, Calcium hydroxide, reactions 1310-58-3, Potassium hydroxide, reactions 1310-65-2, Lithium hydroxide 1310-73-2, Sodium hydroxide, reactions 7580-67-8, Lithium hydride 7646-69-7, Sodium hydride 7693-26-7, Potassium hydride 7789-78-8, Calcium hydride 17194-00-2, Barium hydroxide
RL: RCT (Reactant); RACT (Reactant or reagent)
(cyclization agent; preparation of bactericidal (-) piperazinylpyridobenzoxazine derivs. via cyclization of a 2-aminomethylene-3-oxo-3-phenylpropionate intermediate)

IT 56-34-8, Tetraethylammonium chloride 64-20-0, Tetramethylammonium bromide 68-05-3, Tetraethylammonium iodide 75-57-0, Tetramethylammonium chloride 75-58-1, Tetramethylammonium iodide 311-28-4, Tetrabutylammonium iodide 373-68-2, Tetramethylammonium fluoride 429-41-4, Tetrabutylammonium fluoride 631-40-3, Tetrapropylammonium iodide 665-46-3, Tetraethylammonium fluoride

866-97-7, Tetrapentylammonium bromide 1112-67-0, Tetrabutylammonium chloride 1643-19-2, Tetrabutylammonium bromide 1941-30-6, Tetrapropylammonium bromide 2498-20-6, Tetrapentylammonium iodide 7681-49-4, Sodium fluoride, reactions 7789-23-3, Potassium fluoride 7789-75-5, Calcium fluoride, reactions 13400-13-0, Cesium fluoride
RL: RCT (Reactant); RACT (Reactant or reagent)
(desilylation agent; preparation of bactericidal (-) piperazinylpyridobenzoxazine derivs. via cyclization of a 2-aminomethylene-3-oxo-3-phenylpropionate intermediate)

IT 100986-89-8P 180529-25-3P 180529-26-4P 180682-81-9P 180682-82-0P 180682-83-1P 180682-84-2P 180682-85-3P 180682-86-4P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bactericidal (-) piperazinylpyridobenzoxazine derivs. via cyclization of a 2-aminomethylene-3-oxo-3-phenylpropionate intermediate)

IT **100986-85-4P** 117707-40-1P
RL: **IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)**
(preparation of bactericidal (-) piperazinylpyridobenzoxazine derivs. via cyclization of a 2-aminomethylene-3-oxo-3-phenylpropionate intermediate)

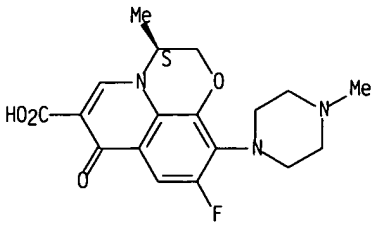
IT 109-01-3, N-Methylpiperazine 110-85-0, Piperazine, reactions 623-47-2, Ethyl propiolate 2749-11-3, (+)-2-Amino-1-propanol 94695-48-4, 2,3,4,5-Tetrafluorobenzoyl chloride 138938-63-3 138938-64-4 173589-92-9, 3,4,5-Trifluoro-2-nitrobenzoyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of bactericidal (-) piperazinylpyridobenzoxazine derivs. via cyclization of a 2-aminomethylene-3-oxo-3-phenylpropionate intermediate)

IT 67-68-5, Dimethyl sulfoxide, uses 68-12-2, Dimethylformamide, uses **75-05-8, Acetonitrile**, uses 109-99-9, Tetrahydrofuran, uses 110-86-1, Pyridine, uses 123-91-1, Dioxane, uses 126-33-0, Sulfolane 127-19-5, Dimethylacetamide 872-50-4, N-Methylpyrrolidone, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; preparation of bactericidal (-) piperazinylpyridobenzoxazine derivs. via cyclization of a 2-aminomethylene-3-oxo-3-phenylpropionate intermediate)

IT **100986-85-4P**
RL: **IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)**
(preparation of bactericidal (-) piperazinylpyridobenzoxazine derivs. via cyclization of a 2-aminomethylene-3-oxo-3-phenylpropionate intermediate)

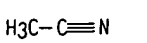
RN 100986-85-4 HCAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid, 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).




IT **75-05-8, Acetonitrile**, uses
RL: NUU (Other use, unclassified); USES (Uses)

(solvent; preparation of bactericidal (-) piperazinylpyridobenzoxazine derivs. via cyclization of a 2-aminomethylene-3-oxo-3-phenylpropionate intermediate)
RN 75-05-8 HCAPLUS
CN Acetonitrile (8CI, 9CI) (CA INDEX NAME)



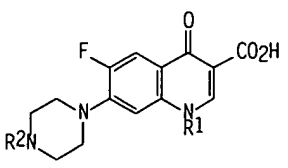
L39 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1992:194351** HCAPLUS
DN 116:194351
ED Entered STN: 16 May 1992
TI Preparation of piperazinylquinolone derivatives
PA Korea Institute of Science and Technology, S. Korea
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07D215-56
ICS A61K031-47; C07D498-06; C07F007-10
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | JP 03279361 | A2 | 19911210 | JP 1990-252044 | 19900925 <-- |
| | JP 07005562 | B4 | 19950125 | | |
| | DE 4100855 | A1 | 19911002 | DE 1991-4100855 | 19910114 <-- |
| PRAI | KR 1990-4115 | A | 19900327 <-- | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| JP 03279361 | ICM | C07D215-56 |
| | ICS | A61K031-47; C07D498-06; C07F007-10 |

OS CASREACT 116:194351; MARPAT 116:194351
GI



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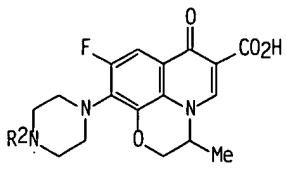
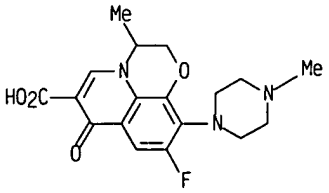


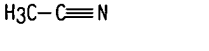
II

AB Title compound I and II (R1 = alkyl, cycloalkyl; R2 = H, alkyl), useful as bactericides, were prepared Thus, stirring 1-ethyl-6-fluoro-7-chloro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid with 1-(tert-butyldimethylsilyl)piperazine and tetrabutylammonium fluoride trihydrate in pyridine at 80.degree. for 2 h gave 90% I (R1 = Et, R2 = H).
ST piperazinylquinolonecarboxylate; pyridobenzoxazinecarboxylate piperazinyl; quinolonecarboxylate prepn bactericide
IT Bactericides, Disinfectants, and Antiseptics
(piperazinylquinolonecarboxylates)
IT 138938-63-3 138938-64-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(amination by, of haloquinoline)
IT 87749-50-6, Tetrabutylammonium fluoride trihydrate
RL: RCT (Reactant); RACT (Reactant or reagent)
(amination of haloquinoline with (butyldimethylsilyl)piperazine in

presence of)
IT 68077-26-9 82419-35-0 86393-33-1 93107-30-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(amination of, with (butyldimethylsilyl)piperazine)
IT 27001-68-9P 70458-92-3P 70458-96-7P **82419-36-1P**
93107-11-0P
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of)
IT 109-01-3, 1-Methylpiperazine 110-85-0, Piperazine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(silylation of, with tert-butyldimethylsilyl chloride)
IT 67-68-5, Dimethyl sulfoxide, uses 68-12-2, Dimethylformamide, uses
**75-05-8, Acetonitrile**, uses 110-86-1, Pyridine, uses
126-33-0, Sulfolane
RL: USES (Uses)
(solvent, for amination of haloquinoline with
(butyldimethylsilyl)piperazine in presence of tetrabutylammonium
fluoride)
IT **82419-36-1P**
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of)
RN 82419-36-1 HCAPLUS
CN 7H-Pyrido[1,2,3-de]-1,4-benzoxazine-6-carboxylic acid,
9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo- (9CI)
(CA INDEX NAME)




IT **75-05-8, Acetonitrile**, uses
RL: USES (Uses)
(solvent, for amination of haloquinoline with
(butyldimethylsilyl)piperazine in presence of tetrabutylammonium
fluoride)
RN 75-05-8 HCAPLUS
CN Acetonitrile (8CI, 9CI) (CA INDEX NAME)

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